PEDIATRIC RSV PATIENTS:
RADIOGRAPHIC FINDINGS ON ADMISSION AND CLINICAL OUTCOMES

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Abstract

Introduction: Respiratory Syncytial Virus (RSV) is a common cause of respiratory tract infections in children during winter and carries a large burden of disease. Clinical risk factors have been identified and used by clinicians to predict severity of RSV in the pediatric population. However, despite the magnitude of disease burden on the pediatric population, limited studies have attempted to correlate radiographic findings on admission with severity of clinical course.

Research Question: Is there a correlation between specific radiographic features of an admission chest X-ray and clinical outcomes of pediatric patients admitted for RSV respiratory tract infection?

Methods: A retrospective chart review of a total of 400 patients admitted between October 2013 through May 2016 was performed by three trained reviewers. Patients admitted with various ICD-9 codes for RSV infection confirmed by lab data were enrolled. Admission Chest Radiographic findings of 296 pediatric patients were reviewed independently by a radiology resident and board-certified radiologist that were aware of the patients' RSV status, but blinded to prior imaging interpretation and clinical presentation. Chest radiographs were read as either normal or abnormal. Abnormal radiographs were reported as hyperinflation, pleural disease, adenopathy, interstitial prominence, airspace opacity, or any combination of the above. Clinical and radiographic trends were evaluated for association with severity of RSV presentation. Severity was defined as hospitalization > 2 days, PICU admission, or mechanical ventilation during hospitalization.

Results: Admission chest radiographs of 296 patients were analyzed. A 'severe' clinical course was defined as hospital stay for more than 2 days, PICU admission, and/or ventilator support (n=122 [41.2 %]). A 'not severe' clinical course was defined by absence of the previous criteria (n=174 [58.8%]). The most common abnormal chest radiograph findings were: interstitial prominence (n=182 [61.5%]), airspace opacity (n=106 [35.8%]), and hyperinflation (n=78 [26.3%]). 49% of patients with a severe clinical course demonstrated airspace opacity, compared to only 26% of patients with a not severe clinical course (p-value <0.001). In addition, 33% of patients with a severe clinical course demonstrated hyperinflation, compared to 22% of

patients with a not severe clinical course (p-value = 0.044). Interstitial prominence was seen in 62% and 61% of patients with severe and not severe clinical courses, respectively (p-value = 0.907). Pleural disease (n=6 [2.0%]) and adenopathy (n=3[1.0%]) were uncommon and thus, not statistically significant.

Conclusion: The radiographic findings found to be independently associated with a severe clinical outcome in RSV positive patients were hyperinflation and airspace opacity. Future research should focus on a predicative model that can provide prognostic clinical outcomes based on initial radiographic findings.

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Introduction

Respiratory Syncytial Virus (RSV) is a common cause of upper and lower respiratory tract infections in the first 5 years of life.[1,2] Incidence of RSV bronchiolitis in children increases in the late fall and winter months when infections with the virus become more common.[1,3] Symptoms of infection apart from respiratory distress can include fever, rhinorrhea, irritability, and poor feeding.[1] Severity can range from a very mild upper respiratory infection, to significant respiratory distress and hypoxia necessitating hospitalization.[1] The variable presentation of this disease can lead to a diagnostic dilemma in delineating RSV infection from other infectious entities such as bacterial pneumonia, viral upper respiratory tract infection, acute otitis media, and sinusitis. Even after microbiologic confirmation, clinicians may feel compelled upon evaluation of the patient to obtain chest radiographs to exclude a bacterial process.[3,4] Our retrospective study evaluated the demographics, clinical course and outcome of patients with PCR-confirmed RSV bronchiolitis. Additionally, we examined the clinical findings as they relate to the severity of radiographic features seen on chest x-ray. The goal was to find if there is a correlation between specific radiographic features of an admission Chest X-Ray and clinical outcomes of pediatric patients admitted for RSV respiratory tract infection

Methods

Maricopa Medical Center (MMC) is a Public Safety Network tertiary general hospital in Phoenix, AZ that is comprised of 449 beds. We performed a retrospective study on children 0-18 years who were admitted to Maricopa Medical Center due to RSV infection between October 2013 and May 2016. October to May period is the peak of RSV season in our community and by selecting this period, vast majority of patients were enrolled. MMC included one pediatric floor with 34 inpatient beds and 12 PICU beds.

Pediatric patients between 0-18 years of age who were admitted to the inpatient floor or PICU at MMC were reviewed. Patients were identified using ICD-9 discharge codes for RSV respiratory tract infections. A positive RSV infection was defined by either PCR or direct florescent antibody (DFA) from a nasopharyngeal swab. A total of 436 patient charts were reviewed and 400 patients met eligibility criteria and were enrolled. Of those enrolled, 296 patients had Chest X-rays independently reviewed.

Chest radiographs were reviewed independently by a radiology resident and board-certified radiologist that were aware of the patients' RSV status, but blinded to prior imaging interpretation and clinical presentation. All chest radiographs were taken using an anteroposterior or posteroanterior projection with a portion including a lateral projection. Chest radiographs were read as either normal or abnormal. Abnormal radiographs were reported as hyperinflation, pleural effusion, adenopathy, interstitial prominence, airspace opacity, and combinations of the above. Airspace opacities were further characterized by laterality (unilateral vs bilateral) and percent of total bilateral lung involved (<10%, 10-50%, and >50%). Interstitial prominence was defined as peripheral, central, and/or peribronchial interstitial prominence. Hyperinflation was defined as increased pulmonary lucency, diaphragmatic flattening, and increased rib count projecting over the lungs (Figure 1).

Severe RSV cases were defined as hospitalizations greater than 2 days, patients admitted to the intensive care unit, and/or patients requiring ventilator support. Bivariate associations between clinical and radiological characteristics of the patients and whether the cases were severe or non-severe were evaluated using Fisher’s exact two-sided P values.

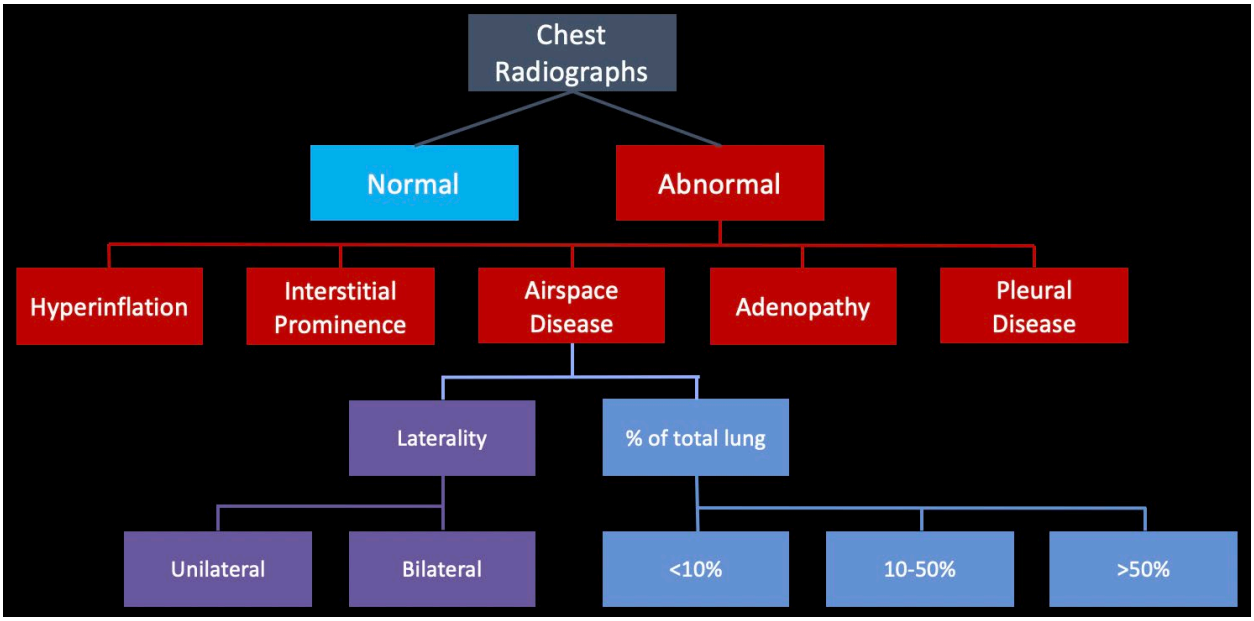

Figure 1. Radiological Review of RSV Admissions. Abnormal radiographs were reported as hyperinflation, interstitial prominence, airspace disease, adenopathy, pleural disease, and any combination of the above. Airspace opacities were further characterized by laterality (unilateral or bilateral) and percentage of total lung involved (<10%, 10-50%, and >50%).

Results

A total of 400 patients were confirmed to be RSV positive by DFA or PCR. Chest X-rays were performed on 296 patients that were independently reviewed. Clinical findings included: cough (97%), rhinorrhea or congestion (93%), fever (78.5%), hypoxia (44.8%), wheezing (35.8%), altered mental status (1.5%), and hypotension (1.0%) (Table 1). In the severe cases of RSV, 64.7% of patients had hypoxia compared to 32.0% in non-severe cases ($p < 0.001$) (Table 2).

The median age of patients who met criteria for severe disease was 2.7 years compared to 1.7 years for those with non-severe disease. The average length of stay for patients who required ventilator support was 12.7 days compared to 2.6 days for those who did not need mechanical ventilation.

The most common abnormal chest radiograph findings were: interstitial prominence (61.5%), airspace opacity (35.8%), and hyperinflation (26.3%) (Table 3). 49% of patients with a severe clinical course demonstrated airspace opacity, compared to only 26% of patients with a non-severe clinical course (p-value <0.001). Unilateral airspace opacity was more common, affecting 23.3% of patients, while bilateral airspace opacity was only found in 12% of patients. Of the patients with air space opacities 18.6% patients presented with airspace opacity affecting <10% of total lung, 15.2% affecting 10-50% of total lung, and 3.7% affecting >50% of total lung.

In addition, 33% of patients with a severe clinical course demonstrated hyperinflation, compared to 22% of patients with a non-severe clinical course (p-value = 0.044). Interstitial prominence was seen in 62% and 61% of patients with severe and non-severe clinical courses, respectively (p-value = 0.907). Pleural disease (2.0%) and adenopathy (1.0%) were uncommon. Complications of pneumothorax or pneumomediastinum were not found in the sample studied.

Clinical Findings	No. of patients[P]
Fever	314 (78.5)
Cough	388 (97.0)
Congestion or Rhinorrhea	372 (93.0)
Wheezing	143 (35.8)
Hypoxia[*]	179 (44.8)
Altered Mental Status	6 (1.5)
Hypotension[+]	3 (1.0)
Acute Otitis Media	71 (17.8)
Antibiotics	201 (50.3)
Albuterol	221 (55.3)
Ventilator Support	9 (2.3)
History of Asthma	52 (13.0)
Family History of Asthma	70 (17.5)

Table 1. Overall Frequency of Clinical Findings. *Hypoxia: Requiring supplemental O2 or SpO2 <93%.

Features of patients		Not severe (%)	Severe (%)	Total* (%)	P- Value
CLINICAL (n=400)	Cough	240 (98.4)	148 (94.9)	388 (97.0)	0.068
	Rhinorrhea or congestion	234 (95.9)	138 (88.5)	372 (93.0)	0.008
	Wheezing	82 (33.6)	61 (39.1)	143 (35.8)	0.286
	Hypoxia (requiring O2 or SpO2 <93%)	78 (32.0)	101 (64.7)	179 (44.8)	<0.001
	Altered Mental Status	1 (0.4)	5 (3.2)	6 (1.5)	0.035
	Hypotension	0	3 (1.9)	3 (0.8)	0.118
	Otitis	48 (19.7)	23 (14.7)	71 (17.8)	0.439
	Antibiotics	113 (46.3)	88 (56.4)	201 (50.3)	0.052
	Albuterol	127 (52.0)	94 (60.3)	221 (55.3)	0.122
	History of Asthma	27 (11.1)	25 (16.0)	52 (13.0)	0.171
	Family History of Asthma	41 (16.8)	29 (18.6)	70 (17.5)	0.720
	Chest -ray recorded	183 (75.0)	126 (80.8)	309 (77.3)	0.221
RADIOLOGY (n=296)	Normal	29 (15.8)	12 (9.5)	41 (13.3)	0.126
	Hyperinflation	38 (20.8)	40 (31.7)	78 (25.2)	0.033
	Pleural Disease	2 (1.1)	4 (3.2)	6 (1.9)	0.230
	Adenopathy	1 (0.5)	2 (1.6)	3 (1.0)	0.569
	Interstitial Prominence	106 (57.9)	76 (60.3)	182 (58.9)	0.725
	Airspace Opacity	46 (25.1)	60 (47.6)	106 (34.3)	<0.001
	Unilateral	31 (16.9)	38 (30.2)	69 (22.3)	0.008
	<10%	24 (13.1)	31 (24.6)	55 (17.8)	0.010
	10-50%	17 (9.3)	28 (22.2)	45 (14.6)	0.003
	>50%	7 (3.8)	4 (3.2)	11 (3.6)	>0.999

Table 2. Comparison of Clinical and Radiographic Findings in the Severe and Non-severe Presentations of RSV.

Radiological Findings	No. of Chest X-rays[P]
Chest X-ray	296 (74.0)
Normal Radiology	41 (13.9)
Hyperinflation	78 (25.2)
Interstitial prominence	182 (61.5)
Pleural Disease	6 (2.1)
Adenopathy	3 (1.0)
Airspace Opacity	106 (35.8)
Unilateral	69 (23.3)
<10%	55 (18.6)
10-15%	45 (15.2)
>50%	11 (3.7)

Table 3. Overall Frequency of Radiographic Findings. P: Percentage of total chest x-rays reviewed.

Discussion

Well-studied clinical risk factors have been identified and used by clinicians to predict severity of RSV pathogenesis in the pediatric population.[5,6,7,8,9] However, despite the magnitude of disease burden on the pediatric population, there are limited studies which correlate admission radiographic findings with severity of clinical course.[10] This study focuses on the clinical and radiographic findings associated with severity of RSV manifestations in a community hospital in Phoenix, Arizona serving a low socioeconomic status and largely Hispanic population.

Analyses of common clinical symptoms associated with RSV infection, such as fever, cough, rhinorrhea and congestion correlate with other studies that have found similar rates of such symptoms.[11,12,13] We also found that less common findings in RSV infection such as altered mental status and hypotension were less prevalent in our study population. In addition, in our group we found the overall prevalence of asthma to be only 13%, and wheezing to be present 35.8% of the time in patients admitted with RSV. Albuterol was used 55.3% of the time correlating with the overuse of beta-agonists in RSV bronchiolitis or RSV pneumonia.[14]

The median age of those with severe (2.7) and non-severe infection (1.7) is higher in this study due to the inclusion of a wider age range compared to other studies that tended to focus on children 2 and under, the typical age range for symptomatic RSV bronchiolitis.[16,17]

Hypoxia was significantly higher in the severe group (64.7%) compared to the non-severe group (32%). In a previous study, hypoxia had a predictive value on outcome and was associated with an increase in ICU admission, oxygen need and length of hospital stay in RSV bronchiolitis.[3] Additionally, we found that rhinorrhea or congestion to be highly prevalent in both the severe and non-severe group though slightly more prevalent in the non-severe group (95.9%) compared to the severe group (88.5%) (p-value = 0.008).

We found that 49.2% of all patients with a severe clinical outcome were found to have airspace opacity on chest radiographs (p-value <0.001). Similarly, other studies have reported that newborns with a consolidation chest pattern had more severe disease with greater need for supplemental oxygen, respiratory support, invasive mechanical ventilation, and longer

length of stay in the NICU.[10,18] Another study reported that any abnormal chest radiograph was more prevalent in the sicker and younger groups among RSV-infected children.[19] Likewise, our study showed that an overwhelming 90.2% of patients with an abnormal chest radiograph on admission had severe clinical outcomes. We further showed that as much as 32.8% of all patients with a severe clinical outcome demonstrated hyperinflation on chest radiographs (p-value 0.044).

Unilateral lung opacification on admission chest radiograph has been reported in up to 81% of adult RSV patients.[20] In contrast, 23.3% of children in our study and 7.1% in another study had a unilateral airspace opacity, demonstrating a significant difference in radiographic disease presentation between pediatric and adult patients.[21]

There are some limitations to our study. The first significant limitation includes the bias to introduced by the reviewing radiologists' knowledge of the RSV status of all patients. This bias is suggested by comparing other fully blinded studies which reported a higher percentage of 'normal' chest radiographs, ranging from 22-30%, compared to our finding of 13.9%.[10,22] Second, follow up chest radiographs performed after admission were not included in the study, therefore, data on the percent of patients with normal chest radiographs progressing into abnormal radiographs is not available.

Future Direction

Future research should focus on creating a predicative model that can provide prognostic clinical outcomes based on initial clinical and radiographic findings. While we found that hypoxia (p-value <0.001), airspace opacity (p-value <0.001) and hyperinflation (p-value = 0.044) are associated with severe clinical outcomes in RSV positive patients, further study on a larger, more heterogeneous population is needed. The implications of a predictive model are such that a patient would receive an escalated treatment on admission with the focus to decrease mortality, duration of symptoms, and length of hospital stay.

Conclusion

In summary, the most common radiographic findings were interstitial prominence, hyperinflation and airspace opacity. The clinical symptom of hypoxia, as well as radiographic findings of hyperinflation and airspace opacity, may be predictors of poorer outcomes for patients with RSV infection. If a patient presents with hypoxia, hyperinflation or airspace opacity, clinicians should consider escalating treatment and pursuing more aggressive methods prior to deterioration of condition, possibly shortening hospital stay, reducing PICU admission, and/or decreasing need for ventilator support. Combining data from this study with large scale prospective studies can be used to generate a clinical predictor algorithm for patients with RSV infection.

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